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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/776,935	12/22/1998	JACQUES DUMAS	BAYER 12P1	7400

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MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
ARLINGTON COURTHOUSE PLAZA I
2200 CLARENDON BOULEVARD
SUITE 1400
ARLINGTON, VA 22201

EXAMINER	
MITCHELL, GREGORY W	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 12/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/776,935	DUMAS, JACQUES	
	Examiner	Art Unit	
	Gregory W. Mitchell	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-24,26 and 30-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) 17-24, 26 and 30-32 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the Remarks and Amendments filed October 20, 2005 in response to the final rejection mailed on June 15, 2005. Prosecution is, hereby, reopened. Claims 17-19, 22, 26 and 30-32 have been amended. Claims 17-24, 26 and 30-32 are pending and are examined herein.

Applicant's amendments have necessitated the withdrawal of the rejections based on Creswell et al. (USPN 5162360). The following rejections now apply.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-19, 22, 26 and 30-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547,

the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1). ***The Nature of the Invention***:

The rejected claim(s) is/are drawn to an invention which pertains to the treatment of rheumatoid arthritis with a heterocyclic substituted urea.

(2). ***Breadth of the Claims***:

The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. The claims encompass a treatment comprising the administration *any* urea encompassed by the formula illustrated by the broad generic structure of formula I. The nature of the invention is complex in that it potentially encompasses a vast number of compounds. For example, when B is phenyl, X is an amide and A is a diazole, R5 and R5' can be independently selected from more than 43 groups; R1 can be selected from 34 groups; and R1' can be selected from 16 groups (which may, in turn, be substituted with more than 100 different groups in various numbers and patterns). A basic look at a single variable of what A, B and Xn (when n is 1) may be leads to variations numbering in excess of (43x43x34x16x100) 100 million possibilities. It is noted that A may be selected from at least 26 groups; B is selected

from 3 groups; n is 0-3; and X is selected from at least 88 different groups (many of which may be substituted with the at least 43 groups of R5 and R5').

(3). ***Guidance of the Specification***:

The guidance given by the specification as to what types of ureas would be useful in a method of the instant invention is limited. Applicant discloses 38 different ureas as ureas useful in *inhibiting p38*. The specification does not teach that the scope of the invention is limited to these ureas and the claims do not claim a method of inhibiting p38, however.

(4). ***Working Examples***:

As discussed above, the working examples show 38 compounds that are capable of inhibiting p38. None are shown to be actually effective at treating rheumatoid arthritis.

(5). ***State of the Art***:

Applicant's assessment of the prior art indicates that inhibition p38 has been shown to inhibit cytokine production (e.g. TNFα, IL-1, IL-6, IL-8) and that TNFα has been linked to rheumatoid arthritis. There is no indication that inhibition of p38 invariably inhibits each of the cytokines listed (as each are simply examples), nor is there any indication that the inhibition of p38 would invariably lead to the treatment of rheumatoid arthritis. Even if we were to assume that an inhibition of p38 would lead to

the desired inhibition of TNFα, a link between TNFα production and rheumatoid arthritis doesn't mean that any inhibition of TNFα would treat the rheumatoid arthritis. It is further noted that the specification likewise indicates that TNFα production is linked to numerous other diseases (see pages 2-5 of the specification).

(6). ***Predictability of the Art***:

It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839 (1970). In the instant case, as discussed above, there is a vast number of compounds encompassed by the claims wherein only 38 of them have been shown to be effective at inhibiting p38. Furthermore, there is no evidence that the compounds actually treat rheumatoid arthritis; it is simply postulated that because these compounds inhibit p38 that they will in turn inhibit TNFα and that they will in turn treat rheumatoid arthritis.

Moreover, one of skill in the art would recognize that it is highly unpredictable in regard to therapeutical effects, side effects, and especially serious toxicity that may be generated by drug-drug inerteractions when and/or after adminstering to a host (e.g., a human) any compound represented by formula I. See "Goodman & Gilman's The Pharmacological Basis of Therapeutics" regarding possible drug-drug interactions (9th ed., 1996), page 51 in particular. *Goodman & Gilman* teaches that "The frequency of significant beneficial or adverse drug interactions is unknown" (see the bottom of the left column of page 51) and that "Recognition of beneficial effects and recognition of and

prevention of adverse drug interactions require a thorough knowledge of the intended and possible effects of drugs that are prescribed" and that "The most important adverse drug-drug interactions occur with drugs that have serious toxicity and a low therapeutic index, such that relatively small changes in drug level can have significant adverse consequences" (see the right of page 51) (emphasis added). In the instant case, in the absence of fully recognizing the identity of the member genus herein, one of skill in the art would not be able to fully predict possible adverse drug-drug interactions occurring with many combinations of any compounds having the claimed functional properties in the pharaceutical compositions herein. Thus, the teachings of *Goodman & Gilman* clearly support that the instant claimed invention is highly unpredictable.

(7). ***The Quantity of Experimentation Necessary***:

The specification fails to provide sufficient support of the broad use of any compound represented by formula I. As a result, one of skill in the art would be forced to perform an exhaustive search for the embodiments of any drugs having the function recited in the instant claim suitable to practice the claimed invention. Furthermore, one of skill in the art would have to determine not only which compounds inhibit p38, but which compounds actually treat rheumatoid arthritis.

Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory W Mitchell whose telephone number is 571-272-2907. The examiner can normally be reached on M-F, 8:30 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

gwm

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER